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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/482,788	01/13/2000	Randy m Berka	5778.200-US	7465

25907 7590 11/27/2002

NOVOZYMES BIOTECH, INC.  
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DAVIS, CA 95616

EXAMINER

RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 11/27/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application N .

09/482,788

Applicant(s)

BERKA ET AL.

Examiner

Delia M. Ramirez

Art Unit

1652

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 29 October 2002 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 29 October 2002. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: none.Claim(s) objected to: none.Claim(s) rejected: 98-123.Claim(s) withdrawn from consideration: none.

8. ☐ The proposed drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

### **ADVISORY ACTION**

1. Claims 98-123 are pending.

2. The request for entering new claims 98-123 and arguments filed on 10/29/2002 under 37 CFR 1.116 in reply to the Final Action Paper No. 10 mailed on 4/23/2002 are acknowledged.

New claims 98-123 will be entered since they simplify the issues for appeal. However, entry of these amendments is not deemed sufficient to place the application in condition for allowance for the following reasons.

3. Applicants argue that a previous 35 USC 112, second paragraph rejection applied to now cancelled claim 88 should be withdrawn since the intended meaning of the term "third" does not relate to a location or a position but relates to the modification. In regard to 35 USC 112, first paragraph rejections of cancelled claims 70-97, Applicants assert that the claimed invention was adequately described by the specification in view of the provided examples which disclose how to disrupt genes encoding cyclohexadepsipeptide synthetases in *Fusarium venenatum* cells and how to express a secreted polypeptide in such cell. Furthermore, Applicants argue that knowledge of the sequence of a gene or which modifications in such gene would lead to deficient production of cyclohexadepsipeptides is not needed in view of Hermann et al. In addition, Applicants argue that the specification is enabling for the claimed invention for the reasons discussed above in further in view of the 59% sequence identity of Applicant's cyclohexadepsipeptide synthetase *Fusarium venenatum* gene and the *Fusarium scirpi* ennatin synthetase gene. Also, Applicants assert that since genes from other *Fusarium* cells encoding ennatin synthetase and D-hydroxyisovalerate dehydrogenase are known in the art, conserved

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regions of such genes can be used to disrupt similar genes in other cells. In regard to 35 USC 103(a) obviousness rejections applied to claims 70-72, 77-78, 80, 86-87, 91-93 and 95, Applicants argue that the combined teachings of Herrmann et al. and Tsuchiya et al. do not render the claimed invention obvious since none of the cited references teach or suggest that a cyclohexadepsipeptide deficient *Fusarium* can be used as a host cell to produced a secreted heterologous protein. It is Applicant's opinion that the Examiner has applied hindsight reconstruction in the instant rejection.

4. It is noted that new claims 98-123 are still directed to the same subject matter as that of cancelled claims 70-97 except that the claims are now limited to mutant *Fusarium* cells.

5. Claims 98-123 would be rejected under 35 USC 112, second paragraph, 112, first paragraph and 103(a) for the reasons of record.

6. While Applicant's arguments relate to rejections of claims which are now cancelled, they have been considered since they are still applicable to newly added claims 98-123. However, these arguments are not persuasive to overcome the rejections which would be applied to newly added claims 98-123. The term "third" in newly added claim 114 is indefinite for the reasons of record. While the genus of filamentous fungal cells have been limited to *Fusarium* cells, there is still not adequate written description of the claimed invention since there is no description of the genus of modifications as encompassed by the claims which would lead to any mutant *Fusarium* cell to produce less cyclohexadepsipeptides. Arguments in regard to the use of conserved regions and the use of Applicant's SEQ ID NO: 1 and 2 to target genes involved in cyclohexadepsipeptide synthesis are not persuasive since the state of the art clearly teaches the unpredictability of using sequence homology to isolate polynucleotides/polypeptides of similar

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function as already discussed. Moreover, the specification does not disclose which are the conserved regions that are indicative of cyclohexadepsipeptide synthetase, enniatin synthetase or D-hydroxyisovalerate dehydrogenase activity in other *Fusarium* cells.

7. In response to Applicant's arguments in regard to the 35 USC 103(a) rejections that there is no suggestion in either reference to combine their teachings, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as indicated in previous Office Action Paper No. 10, mailed on 4/23/2002, one of skill in the art is motivated to produce secreted heterologous proteins with the mutant *Fusarium* cell of Herrmann et al. because it is well known in the art that secretion of heterologous proteins is advantageous as it allows for faster recovery of the desired protein. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

8. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: NONE

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Claims(s) objected to: NONE

Claim(s) rejected: 98-123

Claim(s) withdrawn from consideration: NONE

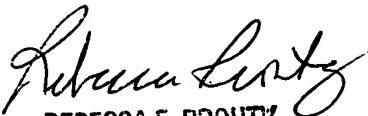
9. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

10. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

  
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PRIMARY EXAMINER  
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